(21)

No. 98-1768

IN THE

Supreme Court of the United States

THE BUCKMAN COMPANY,

Petitioner,

v.

PLAINTIFFS' LEGAL COMMITTEE,

Respondent.

ON PETITION FOR A WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE THIRD CIRCUIT

MOTION OF *AMICUS CURIAE* PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA FOR LEAVE TO FILE BRIEF *AMICUS CURIAE* IN SUPPORT OF THE BUCKMAN COMPANY'S PETITION FOR A WRIT OF CERTIORARI AND BRIEF *AMICUS CURIAE*

MARJORIE E. POWELL
ASSISTANT GENERAL COUNSEL
PHARMACEUTICAL RESEARCH
AND MANUFACTURERS OF AMERICA
1100 Fifteenth Street, N.W.
Washington, D.C. 20005
(202) 835-3400

BERT W. REIN
Counsel of Record
DAVID R. HILL
JENNIFER A. SHAH
WILEY, REIN & FIELDING
1776 K Street, N.W.
Washington, D.C. 20006
(202) 719-7000

Attorneys for Amicus Curiae
Pharmaceutical Research and Manufacturers of America

28 pp

The Pharmaceutical Research and Manufacturers of America ("PhRMA") hereby moves, pursuant to Supreme Court Rule 37.2, for leave to file a brief *amicus curiae* in support of The Buckman Company's petition for a writ of certiorari to the United States Court of Appeals for the Third Circuit. PhRMA is filing this motion because respondent has declined to consent to the filing by PhRMA of this *amicus curiae* brief.[1] A copy of the brief is attached.

As is more fully explained on pages 1-2 of the attached brief, PhRMA is a nonprofit association of the country's leading research-based pharmaceutical and biotechnology companies, which are engaged in the development of innovative medicines and medical devices. PhRMA's members are concerned that the lower court's erroneous decision that plaintiffs' "fraud on the agency" claims are not preempted by § 360k of the Medical Device Amendments of 1976, 21 U.S.C. § 360k (1999), to the Federal Food, Drug, and Cosmetic Act of 1938, 21 U.S.C. §§ 301-396 (1999), would, if left standing, have far-reaching and detrimental effects on the medical device and pharmaceutical industries, and on the public health.

PhRMA is uniquely positioned to assist the Court in this case because its members are subject to, and practically impacted by, the state and federal standards governing approval of devices and drugs. From this perspective, PhRMA can advise the Court regarding the disruptive impact of the decision below on the federal approval regime for devices and drugs. In particular, PhRMA can

1. In response to a request for respondent's consent to the filing by PhRMA of an *amicus curiae* brief in support of the petition, respondent's counsel replied verbally, on May 26, 1999, that respondent was declining to provide such consent.

demonstrate that allowing plaintiffs' "fraud on the agency" claims would impose an additional, burdensome state requirement on applicants for device and drug approvals; severely limit access to "substantial equivalency" approvals for medical devices; and reverse long-standing FDA policies regarding the propriety of so-called "off-label" uses of devices and drugs.

PhRMA also is well positioned to describe for the Court the stifling effect that the lower court's decision would have on the already lengthy and expensive development process for devices and drugs. PhRMA can demonstrate that the allowance of "fraud on the agency" claims such as plaintiffs' would significantly hinder the research, development, and sale of both new and "follow-on" devices and drugs, and would reduce the availability of such products to the public.

Accordingly, PhRMA respectfully requests that this Court grant leave to file the attached *amicus curiae* brief.

Respectfully submitted,

MARJORIE E. POWELL
ASSISTANT GENERAL COUNSEL
PHARMACEUTICAL RESEARCH AND MANUFACTURERS OF AMERICA
1100 Fifteenth Street, N.W.
Washington, D.C. 20005
(202) 835-3400

BERT W. REIN
Counsel of Record
DAVID R. HILL
JENNIFER A. SHAH
WILEY, REIN & FIELDING
1776 K Street, N.W.
Washington, D.C. 20006
(202) 719-7000

Attorneys for Amicus Curiae
Pharmaceutical Research and Manufacturers of America

TABLE OF CONTENTS

	Page
Table of Cited Authorities	iii
Interest of *Amicus Curiae*	1
Reasons for Granting the Writ	3
I. The Lower Court's Ruling That The Plaintiffs' "Fraud On The Agency" Claims Are Not Preempted Must Be Reviewed And Reversed.	7
A. Plaintiffs' "Fraud On The Agency" Claims Are Expressly Preempted By The Medical Device Amendments Of 1976.	10
B. Plaintiffs' "Fraud On The Agency" Claims Are Impliedly Preempted Because They Are In Direct Conflict With The Purposes Of The MDA and FDCA.	12
1. Sustaining The "Fraud On The Agency" Claims Alleged By Plaintiffs Would Severely Limit "Substantial Equivalency" Approvals For Medical Devices, And Would Hinder The Research And Development Of New Devices And Drugs.	12

Contents

Page

2. Sustaining Plaintiffs' "Fraud On The Agency" Claims Would Undermine Long-Standing FDA Policies Regarding "Off-Label" Uses. 18

Conclusion 20

TABLE OF CITED AUTHORITIES

Page

Cases:

Freightliner Corp. v. Myrick, 514 U.S. 280 (1995) 12

Hines v. Davidowitz, 312 U.S. 52 (1941) 6, 12, 15

Medtronic, Inc. v. Lohr, 518 U.S. 470 (1996) 3, 7, 12, 13, 15

Mitchell v. Collagen Corp., 126 F.3d 902 (7th Cir. 1997), *cert. denied*, 118 S. Ct. 1300, 140 L. Ed. 2d 467 (1998) 7, 8

Washington Legal Found. v. Friedman, 13 F. Supp. 2d 51 (D.D.C. 1998), *order amended*, 36 F. Supp. 2d 16 (D.D.C. 1999), *and amended*, 36 F. Supp. 2d 418 (D.D.C. 1999) 5, 18

Statutes:

18 U.S.C. § 1001 3

21 U.S.C. §§ 301-396 (1999) 3

21 U.S.C. § 355(j) (1999) 16

21 U.S.C. § 355(j)(i) 16

21 U.S.C. § 360c(i)(1)(A)(1999) 13

Cited Authorities

	Page
21 U.S.C. § 360c(i)(1)(E) (1999)	11
21 U.S.C. § 360e(b)(1)(B) (1999)	13
21 U.S.C. § 360k	3, 6, 8, 11
21 U.S.C. § 360k(a) (1999)	3, 10
21 U.S.C. § 396 (1999)	5
35 U.S.C. § 154 (1994)	2
United States Constitution:	
U.S. Const. art. VI, cl. 2	3
Other Authorities:	
21 C.F.R. § 314.50(c)(2) (1998)	16
21 C.F.R. § 314.92(a) (1998)	16
21 C.F.R. § 314.94(a)(4)	16
21 C.F.R. § 801.4 (1998)	10, 11
21 C.F.R. § 807.87(e) (1998)	5
21 C.F.R. § 807.87(j)	3

Cited Authorities

	Page
21 C.F.R. § 807.92(a)(5) (1998)	5, 13
21 C.F.R. § 807.100	13
21 C.F.R. § 807.100(b)(1) (1998)	13
21 C.F.R. § 814.20(b)(3)(i) (1998)	5
59 Fed. Reg. 59820 (1994)	10, 18
60 Fed. Reg. 51946 (1995)	5
H.R. Rep. No. 94-853 (1976)	15
H.R. Rep. No. 98-857 (1984)	17

INTEREST OF *AMICUS CURIAE*[1]

The Pharmaceutical Research and Manufacturers of America ("PhRMA") is a voluntary, nonprofit association representing the country's leading research-based pharmaceutical and biotechnology companies, which are devoted to inventing medicines that allow patients to lead longer, healthier, and more productive lives.[2] PhRMA's

1. Pursuant to Supreme Court Rule 37.2(a), PhRMA hereby declares that, in response to a request for Respondent's consent to file a brief *amicus curiae*, Respondent's counsel verbally replied, on May 26, 1999, that Respondent was declining to provide such consent. A motion for leave to file a brief *amicus curiae* is attached to this brief. Pursuant to Supreme Court Rule 37.6, PhRMA also hereby declares that counsel for a party did not author this brief in whole or in part, and that no person or entity other than *amicus curiae*, its members, and its counsel has made a monetary contribution to the preparation or submission of this brief.

2. PhRMA's brief is submitted on behalf of PhRMA members Abbott Laboratories, Agouron, Allergan, Inc., Alza Corporation, American Home Products Corporation (and subsidiaries), Amgen, AstraZeneca PLC, Bayer Corporation (and subsidiaries), Biogen, Inc., Boehringer Ingelheim Corporation (and subsidiaries), Bristol-Myers Squibb Company (and subsidiaries), E.I. DuPont de Nemours & Company, Elan Pharmaceuticals, Fujisawa Healthcare, Inc., Genentech, Inc., Genzyme, Inc., Gilead Sciences, Inc., Glaxo Wellcome, Inc., Hoechst Marion Roussel, Hoffman-La Roche, Inc., Johnson & Johnson (and subsidiaries), Knoll Pharmaceutical Company, Eli Lilly and Company, The Liposome Company, Merck & Co., Inc. (and subsidiaries), Novartis Pharmaceuticals Corporation, Nycomed Amersham Imaging, Organon, Inc., Pasteur Merieux Connaught, Pfizer Inc., Pharmacia & Upjohn, The Procter & Gamble Company, Purdue Pharma L.P., Rhone-Poulenc Rorer, Inc., Sanofi Pharmaceuticals, Inc., Schering-Plough Corporation, Schwarz Pharma, Searle, Serono Laboratories, Inc., SmithKline Beecham Corporation (and subsidiaries), Solvay Pharmaceuticals, 3M Pharmaceuticals, and Warner-Lambert Company (and subsidiaries).

member companies invest nearly $24 billion annually in discovering and developing new medicines, leading the way in the search for cures. These companies are the source of the majority of new drugs that are discovered and marketed throughout the world. A number of PhRMA's members also are engaged in the development and sale of medical devices.

PhRMA estimates that, currently, the average cost of developing a single new drug is approximately $500 million. Testing and obtaining FDA approval for a specific indication(s) of a new drug requires approximately fifteen years.[3] The length of this process already significantly cuts into the patent protection period that affords manufacturers their best opportunity to recover these enormous development costs. *See* 35 U.S.C. § 154 (1994). Extending and increasing the cost of the regulatory process by adding pre-approval burdens arising from state law would diminish the economic feasibility of new device and drug development, to the detriment of PhRMA's members and the public health.

PhRMA's members are deeply concerned that the lower court's decision, unless reviewed and reversed, would effectively rewrite long-standing FDA rules governing the approval of new drugs and medical devices. The lower court's decision squarely conflicts with established FDA practice by allowing states to require that applicants for FDA approval, under the threat of fraud liability, claim as "intended uses" all known or foreseeable uses of each new product. Such state-mandated disclosures, unless preempted, would force applicants to establish the safety

3. This total includes time spent on: (1) "pre-clinical" testing; (2) clinical testing of the drug on human populations; and (3) applying for and awaiting final FDA approval.

and efficacy of all known or foreseeable uses in seeking federal approval. The inevitable result of placing these additional state requirements on manufacturers would be to delay, or even eliminate, the availability of many new and competitive devices and drugs.

For these reasons, PhRMA joins The Buckman Company in urging this Court to accept review in this case, and to reverse the lower court's holding on the preemption issues presented for review.

REASONS FOR GRANTING THE WRIT

The lower court upheld plaintiffs' "fraud on the agency" claims against express preemption challenges under § 360k of the Medical Device Amendments of 1976 ("MDA"), 21 U.S.C. § 360k(a) (1999), to the Federal Food, Drug, and Cosmetic Act of 1938 ("FDCA"), 21 U.S.C. §§ 301-396 (1999), and implied preemption challenges under the Supremacy Clause, U.S. Const. art. VI, cl. 2. Appendix to Petition for a Writ of Certiorari, The Buckman Company, No. 98-1768, at 25a (filed May 3, 1999) (hereafter "Petitioner's Appendix"). In so doing, the lower court read this Court's decision in *Medtronic, Inc. v. Lohr*, 518 U.S. 470 (1996), to create a presumption against preemption of claims based on state laws of general applicability. Petitioner's Appendix at 12a-13a. The court also concluded that imposing state fraud liability on petitioner would merely reinforce duties of candor imposed by FDA regulations and the federal criminal code. *Id.* at 13a (citing 21 C.F.R. § 807.87(j); 18 U.S.C. § 1001). Both of these conclusions were erroneous, and led to a misapplication of the MDA's preemption clause that will bring state law and the federal regulatory scheme into direct conflict.

As discussed more fully below, the lower court's primary analytical mistake was its failure to recognize the specific elements of the "fraud on the agency" alleged by plaintiffs. The particular "fraud on the agency" claimed by plaintiffs is the alleged suppression of petitioner's *subjective* intent regarding the uses of the bone screws manufactured by its client, AcroMed Corporation. Plaintiffs claim that petitioner joined in misrepresenting to the FDA that the screws were intended to be used to treat "long bone" injuries of the arms and legs. *Id.* at 8a. In truth, according to the complaint, petitioner understood that the screws would be used for pedicle (spinal) surgery, a use well-established in medical practice, but not approved by the FDA. *Id.* at 8a-9a; *see also id.* at 28a-29a n.1 (Cowen, J., dissenting) (discussing the FDA's recognition that pedicle use of bone screws, while not federally approved, is nonetheless widespread).

According to plaintiffs, petitioner's fraudulent statement regarding "intended use," which was consistent with the labeling and promotional materials submitted to the FDA, resulted in FDA approval of the marketing of AcroMed's screws. *Id.* at 8a-9a. Because the screws were allowed onto the market, physicians were able to use them in pedicle surgeries, notwithstanding the absence of FDA approval of the screws for that use. *Id.* at 9a. Plaintiffs claim that the pedicle surgeries that allegedly caused them harm would never have been performed but for the availability of AcroMed's screws. *Id.*

In considering the preemption questions, the lower court failed to define with precision the fraudulent act at issue. Instead, the court addressed its analysis to "fraud" on a general level, holding that, because federal law prohibits

"fraud," plaintiffs' "fraud on the agency" claims merely paralleled the requirements of federal law. *Id.* at 13a. In making this broad assertion, the lower court overlooked the inevitable divergence it was creating between federal and state device application requirements.

The FDA's long-standing practice in reviewing both medical device and drug applications is to consider the safety and efficacy of those "intended uses" for which a manufacturer seeks labeling and promotional authorization. *See Washington Legal Found. v. Friedman*, 13 F. Supp. 2d 51, 55 (D.D.C. 1998), *order amended*, 36 F. Supp. 2d 16 (D.D.C. 1999), *and amended*, 36 F. Supp. 2d 418 (D.D.C. 1999); *see also* 21 C.F.R. §§ 807.87(e), 807.92(a)(5) and 814.20(b)(3)(i) (1998) (a manufacturer seeking approval of a new device must state the device's "intended uses"). As Judge Cowen noted in dissenting below, the FDA and applicant-manufacturers recognize the possibility, and in some cases the virtual certainty, that devices and drugs approved for one "intended use" will be employed by physicians for other "off-label" uses. Petitioner's Appendix at 28a-29a (Cowen, J., dissenting); *see also Friedman*, 13 F. Supp. 2d at 56 (noting that "off-label" use is "an established aspect of the modern practice of medicine."). Because Congress has disavowed any interest in regulating the practice of medicine, *see* 21 U.S.C. § 396 (1999), the FDA has made no effort to eliminate "off-label" use of approved devices and drugs, and such use has become the standard of care in many fields of medicine. *See, e.g.*, 60 Fed. Reg. 51946, 51947 (1995) (discussing the FDA's recognition, since 1992, that pedicle fixation with bone screws has constituted the standard of care in the surgical community).

Undercutting this established federal practice, the "fraud on the agency" claims upheld below would subject manufacturers to potential state liability (including punitive damages) whenever "off-label" uses of approved products cause harm. Only by disclosing all known or foreseeable uses to the FDA, and undertaking to prove them safe and effective, could a manufacturer avoid the threat of potentially massive "fraud on the agency" liability of the type alleged by plaintiffs. Thus, the existing federal regime — which permits manufacturers to market a product, under controlled labeling and promotional restrictions, so long as *any* safe and effective use is established — would be transformed into a regime in which market access is denied unless *all* known or foreseeable uses are shown to be safe and effective.

As further explained below, the extension of the approval process to unclaimed, but known or foreseeable, uses at the very least adds a state-based requirement to the MDA approval regime, and thus runs afoul of 21 U.S.C. § 360k. In addition, the disclosure requirement effectively imposed by the lower court's decision would slow, and in some cases foreclose, market access for new products, particularly for "follow-on" drugs and devices for which, as here, "off-label" uses are established. This result would contravene the legislative scheme and purposes of the MDA and FDCA, and accordingly should be foreclosed by established principles of implied preemption. *Hines v. Davidowitz*, 312 U.S. 52, 67 (1941).

I.

THE LOWER COURT'S RULING THAT THE PLAINTIFFS' "FRAUD ON THE AGENCY" CLAIMS ARE NOT PREEMPTED MUST BE REVIEWED AND REVERSED.

In analyzing a preemption question, a court must engage in a precise comparison of the conduct required by the state claim with that mandated by federal law. Only in this manner can a reviewing court determine whether the state claim is in conflict with the express mandates of federal law, and/or with the overarching purposes of the federal legislative scheme. *See Medtronic*, 518 U.S. at 504-05 (opinion of Breyer, J.) (stating that state common-law actions may be preempted if they require conduct that is different from or additional to that required by federal law, and positing that a state negligence action based on the use of a 1-inch hearing aid wire should be preempted by a federal regulation requiring 2-inch wires).

This logical, comparative analysis was used by the Seventh Circuit in *Mitchell v. Collagen Corp.*, 126 F.3d 902 (7th Cir. 1997), *cert. denied*, 118 S. Ct. 1300, 140 L. Ed. 2d 467 (1998). The *Mitchell* court recognized:

> [I]n order to determine whether a common law cause of action is preempted by the action of the FDA, it is necessary to examine the state law cause of action at a sufficiently precise level of generality to determine whether the final judgment of the state court would impose on the manufacturer a burden incompatible with the requirements imposed by the FDA.

Id. at 912. The *Mitchell* court engaged in a claim-by-claim comparison of state- and federally-mandated conduct, and found that, to the extent the conduct required by the plaintiffs' strict liability, negligence, mislabeling, misbranding, adulteration, "fraud on the agency" and implied warranty claims was additional to or different from that required under federal law, such claims were preempted by § 360k. *Id.* at 913-15.

In this case, by contrast, the lower court failed to analyze the precise conduct required by plaintiffs' "fraud on the agency" claims. Consequently, it failed accurately to compare such claims with the requirements of the MDA, and with the overarching purposes of the federal regime. As a result of this threshold analytical error, the lower court found several generalized grounds for rejecting preemption of plaintiffs' claims.[4] Analyzed with particularity, however, it becomes evident that plaintiffs' claims are barred by both express and implied preemption principles.

The claims before this court are narrowly defined. They do not allege injury caused by fraudulent marketing, false promotion, mislabeling, or misbranding of AcroMed's bone

4. First, the court apparently concluded that, because plaintiffs' claims alleged "fraud" — which is generally proscribed by federal law — they simply mirrored federal regulations, and did not impose different or additional state law requirements upon applicants for medical device approval. Petitioner's Appendix at 13a. Alternatively, the court concluded that, even if plaintiffs' claims established additional state requirements, such requirements were not specific to petitioner's device, and were therefore not expressly preempted by the MDA. *Id.* Lastly, the court found that allowing a state-based remedy for "fraud" by medical device manufacturers and their agents would not thwart the purposes of the federal regulatory scheme. *Id.* at 16a-17a.

screws. Nor do they involve contentions that the bone screws were defectively manufactured or designed, or that they were used in an improper "off-label" manner. Instead, as discussed above, plaintiffs raise the limited allegation that the *very existence of the screws on the market* — facilitated by petitioner's "fraud on the agency" — caused them "harm."[5]

The particular "fraud on the agency" allegedly perpetrated by petitioner is similarly limited in scope. Plaintiffs do not claim that petitioner falsified any data. They claim instead that petitioner committed "fraud" by failing to disclose to the FDA its subjectively "intended uses" for AcroMed's bone screws. Petitioner's Appendix at 8a-9a.

As such, the narrow preemption question presented by this case is this: Does the MDA expressly or impliedly preempt a state law requirement that applicants for medical device approval disclose to the FDA their subjective intent or knowledge with respect to the known or foreseeable uses to which the device will be put by unrelated persons?

Contrary to the lower court's finding, the answer to this question must be "yes." Plaintiffs' "fraud on the agency" claims are expressly preempted by the MDA, as they would

5. In fact, plaintiffs could not have made any of the above allegations in the lower court because petitioner — the sole party certified on appeal to that court — acted only as a regulatory consultant to AcroMed during the FDA approval process, and did not participate in manufacturing, marketing, or other external activities. *See* Petition at 5-6; Petitioner's Appendix at 8a-9a (describing the plaintiffs' allegations).

impose an additional state requirement of "full disclosure" on applicants for medical device approval. Moreover, plaintiffs' claims are impliedly preempted because they would severely disrupt the federal approval scheme for devices and drugs, and would work against the public health objectives of the MDA and FDCA.

A. Plaintiffs' "Fraud On The Agency" Claims Are Expressly Preempted By The Medical Device Amendments Of 1976.

The preemption clause of the MDA precludes the establishment or continuation of any state requirement with respect to a medical device that is different from, or in addition to, the federal requirements applicable to the device. 21 U.S.C. § 360k(a) (1999). Plaintiffs' "fraud on the agency" claims are preempted under these terms, for allowing such claims would add a state-based requirement to the federal device approval process.

Federal law does not require manufacturers of medical devices (or their agents) to reveal their subjective "intended uses" for a device for which they are seeking FDA approval. In fact, judging "intended use" based on subjective intent is directly contrary to the federal regulatory scheme. The MDA's implementing regulations define "intended use" in an objective fashion. 21 C.F.R. § 801.4 (1998) (providing that the "intended use" of a device is determined by "the objective intent of the persons legally responsible for the labeling of devices."); *see also* 59 Fed. Reg. 59820, 59822 (1994) (acknowledgment by the FDA that "[a] product's intended use is usually primarily a function of the manner in which a company characterizes its product in the marketplace."). Under the regulations, objective intent is

determined by examining the manufacturer's proposed labeling and conduct, not by a speculative inquiry into the subjective expectations or knowledge of the manufacturer or its employees. 21 C.F.R. § 801.4.[6]

Indeed, interpreting the term "intended use" subjectively, or to include unclaimed, but known or foreseeable, uses defies both federal intent and common sense. Neither manufacturers nor the FDA can lawfully control the uses to which their devices are put by healthcare providers. It is irrelevant to the FDA whether a manufacturer subjectively "intends" or desires for any particular "off-label" uses to be adopted. All that is relevant to — and reasonably discernible by — the FDA is the manufacturer's expressed intent, as evidenced by its conduct in labeling, advertising, and marketing its devices. *See id.* Moreover, it would be administratively difficult, if not impossible, for the FDA to determine, at the approval stage, whether a manufacturer has truthfully revealed all of its subjectively intended uses for a product.

Because plaintiffs' "fraud on the agency" claims hold manufacturers liable for failing to make an additional, "subjective intent" disclosure, they impose a requirement under state law that is "in addition to" established federal requirements. Accordingly, such claims are expressly preempted by § 360k.

---

6. In fact, Congress has recently expressly recognized the objective nature of the "intended uses" disclosure. *See* 21 U.S.C. § 360c(i)(1)(E) (1999) ("Any determination by the Secretary of the intended use of a device shall be based upon the proposed labeling submitted in a report for the device under section 360(k) of this title.").

B. Plaintiffs' "Fraud On The Agency" Claims Are Impliedly Preempted Because They Are In Direct Conflict With The Purposes Of The MDA and FDCA.

More fundamentally, plaintiffs' "fraud on the agency" claims inherently clash with and obstruct achievement of the overarching purposes of the MDA and FDCA. Such claims will work to stifle the research and development of new and "follow-on" medical devices and medicines, to the detriment of the general public health.

Under the analysis delineated by this Court, a federal statute impliedly preempts any state law that either actually conflicts with the federal law, or "stands as an obstacle to the accomplishment and execution of the full purposes and objectives of Congress." *Freightliner Corp. v. Myrick*, 514 U.S. 280, 287 (1995) (quoting *Davidowitz*, 312 U.S. at 67). A majority of this Court in *Medtronic* recognized that state law claims against medical device manufacturers could be subject to preemption under these principles. 514 U.S. at 503, 507-08 (plurality opinion and opinion of Breyer, J.). In this case, allowance of "fraud on the agency" claims will have both of these impermissible effects.

1. Sustaining The "Fraud On The Agency" Claims Alleged By Plaintiffs Would Severely Limit "Substantial Equivalency" Approvals For Medical Devices, And Would Hinder The Research And Development Of New Devices And Drugs.

Most strikingly, "fraud on the agency" claims such as plaintiffs' would likely severely hinder the ability of medical device manufacturers to seek expedited "§510(k)" approval

based on a device's "substantial equivalency" to a preexisting device. *See* 21 U.S.C. § 360e(b)(1)(B) (1999). To that extent, such claims would bring state law into direct conflict with the federal legislative scheme, and would frustrate legislative goals by stifling the dissemination of competitive "follow-on" medical devices.

Under § 510(k), a medical device manufacturer seeking to sell a new device may avoid the rigorous "premarket approval" process, and instead obtain expedited FDA approval, by demonstrating that the device is "substantially equivalent" to a preexisting device. *Id.*; *see also Medtronic*, 518 U.S. at 477-79. A manufacturer seeking § 510(k) approval must submit a "premarket notification" to the FDA describing, among other things, the "intended uses" of the device. 21 C.F.R. § 807.92(a)(5) (1998). If the FDA determines that the proposed device is "substantially equivalent" to its predecessor for the specified "intended uses," it will grant approval. *Id.* § 807.100.

Importantly, a manufacturer cannot secure § 510(k) approval for a device with materially different or additional "intended uses" from those of its predecessor. 21 U.S.C. § 360c(i)(1)(A)(1999) ("substantial equivalence" of devices requires that the devices have the same intended uses); 21 C.F.R. § 807.100(b)(1) (1998). Thus, where a new device claims uses in addition to those of its predicate, its manufacturer cannot obtain expedited approval to market the device.

Under the "fraud on the agency" claims alleged by plaintiffs, however, device manufacturers and their agents face potentially massive fraud liability for *failing* to seek approval for all known or foreseeable uses of the devices

they wish to market. Plaintiffs harmed by allegedly known or foreseeable "off-label" uses could allege, as in this case, that the manufacturer "subjectively intended" the device to be put to the use in question, and defrauded the FDA by failing to reveal such intent.

A manufacturer could defend itself from "fraud on the agency" claims such as these only by disclosing to the FDA all known or foreseeable uses, and seeking either approval or "contraindication" labeling therefor. This is because, with respect to any "off-label" use for which labeling is *not* sought, plaintiffs could assert that the manufacturer "subjectively intended" the use to be adopted, and failed to reveal such intent to the FDA.[7] As a result, a manufacturer's only affirmative defenses to a "fraud on the agency" claim would be either: (1) that the manufacturer *did* subjectively intend for the "off-label" use in question to be adopted, *and* disclosed such intent to the FDA by seeking approval for that use; or (2) that the manufacturer *did not* intend such use, and proved as much by seeking "contraindication" labeling.

Practically, to protect themselves from "fraud on the agency" claims of the type plaintiffs allege, manufacturers would be forced to abandon the § 510(k) "substantial equivalency" process, and submit their devices instead to the "premarket approval" process. This would radically

7. Indeed, this is precisely what plaintiffs claim here: despite the fact that the FDA had actual knowledge that the bone screws would be used in pedicle surgery (by virtue of AcroMed's prior applications for such use), plaintiffs maintain that petitioner and AcroMed "defrauded" the FDA in failing to seek approval for that use at the same time they sought approval for "long bone" use. Petitioner's Appendix at 5a, 8a-9a.

change the current trend in device approval applications, *see Medtronic*, 518 U.S. at 479-80 (reporting that, in 1990, 80% of new Class III devices were approved through the § 510(k) mechanism), and would thwart the salutary legislative purposes for which the expedited approval scheme was enacted. *Id.* at 478 (noting that the scheme was intended to "prevent manufacturers of grandfathered devices from monopolizing the market while new devices clear the PMA hurdle, and to ensure that improvements to existing devices can be rapidly introduced into the market[.]").

As a result, plaintiffs' "fraud on the agency" claims would bring state law into irreconcilable conflict with § 510(k), and with the intent of Congress in enacting that amendment to the FDCA. Accordingly, such claims are barred under traditional principles of "conflict" preemption. *See id.* at 507-08 (opinion of Breyer, J.) (citing *Davidowitz*, 312 U.S. at 67).

In addition to directly undermining the § 510(k) process, plaintiffs' "fraud on the agency" claims would interfere with the federal regulatory scheme regarding "breakthrough" device approvals. Because the threat of "fraud on the agency" liability would force manufacturers to rigorously test for all potential uses, disclose their test results to the FDA, and seek labeling therefor, plaintiffs' claims would work to significantly slow the already laborious process of researching, testing, and seeking approval for new, beneficial devices. As a result of this slowing, there would be reduced availability of innovative products to the public. This adverse consequence conflicts with the MDA's goal of ensuring the ready availability of safe and effective medical devices. *See* H.R. Rep. No. 94-853, at 12 (1976).

Additionally, the disruptive effects of the allowance of plaintiffs' "fraud on the agency" claims would likely spill over to the drug approval regime. Drug manufacturers are required, in seeking FDA approval, to list the intended indications of the drug in question. *See* 21 C.F.R. § 314.50(c)(2) (1998). As a result, "fraud on the agency" claims such as those alleged by plaintiffs could (and likely would) be asserted against such manufacturers any time an allegedly known or foreseeable "off-label" use of a drug caused injury. To avoid exposure to "fraud on the agency" claims, drug manufacturers likely would be forced to shoulder the same pre-approval burden as medical device manufacturers – namely, testing and seeking labeling for all known or foreseeable uses of proposed drugs.

As is true with respect to medical devices, "fraud on the agency" liability likely would slow all drug approvals, and severely limit availability of the "abbreviated" approval process for "generic" drugs. Under the FDCA, a drug manufacturer may submit an Abbreviated New Drug Application ("ANDA") seeking expedited FDA approval for a "generic" drug that is essentially identical to a "listed" drug. 21 U.S.C. § 355(j) (1999); 21 C.F.R. § 314.92(a) (1998) (ANDAs may be submitted for drugs that are "identical in active ingredient(s), dosage form, strength, route of administration, and conditions of use[.]"). As is the case under § 510(k), an ANDA may seek approval *only* for the same uses previously approved for the listed drug; manufacturers may not use the application to seek approval for additional uses. 21 U.S.C. § 355(j)(i); 21 C.F.R. § 314.94(a)(4).

If plaintiffs' "fraud on the agency" claims are allowed, however, manufacturers seeking ANDA approval may be

faced with liability for "fraud" if they fail to seek federal approval for all allegedly known or foreseeable uses.[8] Given this significant risk, manufacturers likely would be forced to abandon the ANDA process altogether. The end result – diminished availability of competitive alternative medicines – would be directly at odds with Congress' intent in enacting the ANDA provisions in 1984. *See, e.g.*, H.R. Rep. No. 98-857, pt. 1, at 14 (1984) (stating that the legislation's purpose was "to make available more low cost generic drugs by establishing a generic drug approval procedure for pioneer drugs first approved after 1962.").

In sum, the allowance of plaintiffs' "fraud on the agency" claims would effectively eviscerate approval for "follow-on" medical devices, and would hinder the development and marketing of innovative new devices. These disruptive effects could spill over to the drug approval context. Because plaintiffs' claims would create significant disharmony between state law and the terms and goals of the federal approval scheme, they are impliedly preempted.

---

8. This dilemma frequently would arise in the generic drug context. Once a "brand-name" drug entered the market, physicians would be free to adopt "off-label" uses for the drug. Thus, by the time a generic drug manufacturer submitted an ANDA (in an attempt to provide an alternative to the consuming public), there almost certainly would be known "off-label" uses of the drug. Generic drug manufacturers would risk "fraud on the agency" claims such as plaintiffs', however, if they chose to submit the ANDA in the statutorily required manner — that is, without seeking approval for such "off-label" uses.

2. Sustaining Plaintiffs' "Fraud On The Agency" Claims Would Undermine Long-Standing FDA Policies Regarding "Off-Label" Uses.

In a related respect, plaintiffs' "fraud on the agency" claims would disrupt the delicate balance struck by the FDA with respect to the proper role of manufacturers in facilitating "off-label" uses of approved devices and drugs.

As noted above, the FDA has long accepted "off-label" use as a rational and beneficial part of the practice of medicine. *See* 59 Fed. Reg. 59820, 59821 (1994) (noting that the FDA has long held that " 'unlabeled' uses may be appropriate and rational in certain circumstances, and may, in fact[,] reflect approaches to drug therapy that have been extensively reported in medical literature."); *see also Friedman*, 13 F. Supp. 2d at 55-56. Consequently, such uses are prevalent, especially in important fields such as oncology and pediatrics. *Id.* at 56. In some areas of practice, such uses constitute the standard of good medical care. *Id.*

The FDA, while attempting to regulate the manner and extent to which manufacturers can participate in the development and dissemination of information regarding "off-label" uses, also has recognized the need for adequate information regarding such uses. *See id.* at 56-58. As Judge Cowen stated in dissent, given the FDA's acceptance of "off-label" uses, "difficult and subtle balancing is called for in evaluating manufacturers' roles in the creation and distribution of information about [such] uses[.]" Petitioner's Appendix at 30a; *see also* 59 Fed. Reg. 59820, 59823 (1994).

Plaintiffs' "fraud on the agency" claims would wreak havoc on this balancing by forcing manufacturers, to the extent they are able, to eliminate "off-label" uses entirely. As discussed above, to avoid massive "fraud" liability, manufacturers would seek to include as many uses as possible "on-label." Further, manufacturers would be discouraged from contributing to efforts to study and provide information regarding alternative uses of their products, since such efforts might be viewed as evidence of their "subjective intent" with respect to such uses. Thus, plaintiffs' "fraud on the agency" claims could curtail "off-label" uses in a sweeping and misdirected manner that is discordant with the federal regulatory scheme.

In sum, the injection of plaintiffs' state-based "fraud on the agency" claims into the federal approval process would bring state law into irreconcilable conflict with the MDA and FDCA regimes, and would have significant adverse effects on medical device and drug manufacturers, and on the public health. These effects fully warrant this Court's review and reversal of the lower court's holding that plaintiffs' "fraud on the agency" claims are not preempted.

CONCLUSION

For all of the foregoing reasons, this Court should grant the petition on the questions presented, and reverse the lower court's decision.

Respectfully submitted,

MARJORIE E. POWELL
ASSISTANT GENERAL COUNSEL
PHARMACEUTICAL RESEARCH
AND MANUFACTURERS OF
AMERICA
1100 Fifteenth Street, N.W.
Washington, D.C. 20005
(202) 835-3400

BERT W. REIN
Counsel of Record
DAVID R. HILL
JENNIFER A. SHAH
WILEY, REIN & FIELDING
1776 K Street, N.W.
Washington, D.C. 20006
(202) 719-7000

June 3, 1999

Attorneys for Amicus Curiae
Pharmaceutical Research and Manufacturers of America